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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
CAPUTA, A	
ART UNIT	**PAPER NUMBER**
1817	

DATE MAILED: 11/05/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
08/466,698	Sansonetti et al.
Examiner	**Group Art Unit**
Anthony C. Caputa	1817

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☒ expires *six* months from the mailing date of the final rejection.

b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due two months from the date of the Notice of Appeal filed on _____ (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on *9 Oct 1997* **has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:**

☐ The proposed amendment(s):

☐ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☐ will not be entered because:

☐ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☐ Applicant's response has overcome the following rejection(s):

_____

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
see attachment

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: _____

Claims objected to: _____

Claims rejected: *1-10, 13, and 14*

☐ The proposed drawing correction filed on _____ ☐has ☐has not been approved by the Examiner.

☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ .

☐ Other

ANTHONY C. CAPUTA
PRIMARY EXAMINER
ART UNIT 1817

1. Claims 1-10, 13, and 14 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the Office Action mailed 4/30/97 (see Paper No. 13).

As set previously, it is apparent that numerous modified Shigella are required to practice the claimed invention.

In the instant case the construction of claimed Shigella mutants requires knowledge of the nucleotide sequence of said genes, which regions are responsible for biological activity, and the number of nucleotides which must be deleted or inserted. Due to the limited teaching of the specification and the unpredictable nature of which mutations are useful one skilled in the art can not practice the invention as claimed absent undue experimentation. In view of the foregoing the only means by which applicants can provide an enabling disclosure for the Shigella mutants is by depositing said mutants and limiting the claims to the deposited mutants.

Applicants urge that the specification provides sufficient teachings for one skilled in the art to practice the claimed invention (see page 5 of applicants' response submitted after final dated October 9, 1997-Paper No. 20). Applicants state that the specification teach of methods of modification to employ in order to inactivate the genes. These arguments are not considered persuasive. The decisional law has held the mere recitation in the specification of a broad concept does not necessarily provide a sufficient basis for broadly claiming it (i.e. transposon mutagenesis). See Ex parte Gardner 157 USPQ 162 (Bd. Pat. Appls and Interf. 1967), In re Cavallilo, 127 USPQ 202 (CCPA 1969). The fact that the terms in a claim are the same as those in the specification does not prevent the claims from being rejected as unduly broad if they define subject matter not define subject matter not described to be the actual invention by means of adequate representative samples. See in re Lund, 153 USPQ 625 (CCPA 1967). In the instant case the construction of claimed Shigella mutants requires knowledge of the nucleotide sequence of said genes (iscA, virG, aerobactin, enterochelin), which regions are responsible for biological activity, and the number of nucleotides which must be deleted or inserted. Due to the limited

teaching of the specification and the unpredictable nature of which mutations are useful one skilled in the art can not practice the invention as claimed absent undue experimentation.

While it would appear techniques are known in the art for inactivation, as pointed out by applicants (see pages 2 to 4 of applicants' response submitted after final dated October 9, 1997-Paper No. 20) it is **not** routine in the art to screen for positions within the DNA sequence of the gene so that it does not invade the cells, spread within infected cells, or not produce toxins. Because the specification does **not** disclose :

- which regions of the genes are responsible for biological activity;
- the number of nucleotides which must be deleted or inserted;
- the identity of the genes that are responsible for invading cells, not producing toxins, etc.;
-more than one genes would be expected to be involved in toxin production, spreading, and/or invasion;
- no guidance as to which of the essentially infinite possible choices is likely to be successful;

modifications that can be made to inactivate the genes is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Applicants argue Nassif et al. (see Exhibit 1), Baudry et al. (see Exhibit 2), and Maurelli et al (see Exhibit 3) contain the teachings necessary for screening the *Shigella* genes involved in the invasion of cells, spreading within infected cells, etc.. Applicants arguments are not persuasive. Baudry et al. submitted by applicants (see response submitted after final dated October 9, 1997-Paper No. 20-Exhibit 2) sets forth "The available data indicate that the invasive ability of *S flexerni* is a very complex phenomenon which involves many genes and a large array of polypeptides" and "Whether all these gene products are directly involved in the interaction with the cells, or whether a pool of polypeptides is necessary for transformation and/or correct

positioning of a unique product is yet not known" (see page 3411, last para) . In view of: 1) the statements of Baudey et al pointed out above; 2) the assay procedures of Nassif et al. are only directed to one gene which encodes for aerobactin; 3) case law sets forth the general process of isolating DNA does not mean that the claimed specific compound was precisely envisioned or obvious (see *In re Deuel* 34 USPQ2d 1210 Fed Cir 1995) and; 4) modifications that can be made to inactivate the genes are unpredictable as set forth above the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement is maintained.

Beyond the reasons set forth above, applicants arguments are not sufficient to obviate the rejection in view of *Fliers v. Sugano,* 25 USPQ 2d 1601 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., and Genetics Institute., Inc.,* 18 USPQ 2d 1016 (Fed. Cir. 1991) as set forth in the prior Advisory Action mailed 9/26/97.

2. The prior provisional rejection of claim 13 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending application Serial No. 08/118,100 is maintained for the reasons of record.

Applicants requested to hold this rejection in abeyance until allowable subject matter has been indicated in either case. The Examiner notes that USSN 08/118,100 has been allowed. Until applicants submit a proper terminal disclaimer said rejection is maintained.

3. Any inquiry concerning this communication should be directed to Dr. Anthony C. Caputa, whose telephone number is 703-308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is 703-308-0196.

Papers related to this application may be submitted to Group 1817 by facsimile transmission. Papers should be faxed to Group 1817 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703)-308-4242.

Anthony C. Caputa, Ph.D.
November 5, 1997